

AMENDMENT
US APPLN. NO. 11/034,281

Listings of the claims:

1-11 (Cancelled)

12. (Withdrawn) A recombinant nucleic acid encoding an inhibitor-resistant HCV NS3 protease according to anyone of claim 1.

13. (Withdrawn) A nucleotide probe capable of hybridizing under stringent conditions to a nucleic acid sequence as defined to claim 12.

14. (Withdrawn) A vector incorporating a nucleic acid as defined in claim 12.

15. (Withdrawn) A host cell transfected with the vector as defined in claim 14.

16. (Withdrawn) A method for evaluating HCV NS3 protease activity of inhibitor-resistant NS3 protease, said method comprising the steps of:

- incubating host cells as defined in claim 15 under conditions which cause said protease to be expressed; and
- measuring the replication of said nucleic acid;

wherein the level of replication of said nucleic acid is proportional to the activity of said expressed protease.

17. (Withdrawn) A method for identifying potential a second generation inhibitor of HCV NS3 protease activity comprising:

- incubating host cells as defined in claim 15 under conditions which cause expression of said inhibitor-resistant protease, in the absence of a candidate second generation inhibitor

AMENDMENT
US APPLN. NO. 11/034,281

compound;

• incubating said host cells as defined in claim 15 under conditions which cause expression of said inhibitor-resistant protease, in the presence of a candidate second generation inhibitor compound; and

• measuring the replication of said nucleic acid in the presence and absence of said candidate second generation inhibitor compound,

wherein the level of replication of said nucleic acid is proportional to the activity of said expressed protease, and wherein a decrease in activity of said protease in the presence of a candidate inhibitor compound indicates that said compound inhibits the protease.

18. (Withdrawn) A method for identifying potential a second generation inhibitor of HCV NS3 protease activity comprising:

• incubating an inhibitor-resistant NS3 protease mutant as defined in claim 1 in the presence or absence of a candidate second generation inhibitor compound; and

• measuring the protease activity of said inhibitor-resistant NS3 protease in the presence and absence of said candidate second generation inhibitor compound;

wherein a decrease in activity of said protease in the presence of a candidate second generation inhibitor indicates that said compound inhibits said inhibitor-resistant NS3 protease.

19. (New) A variant HCV NS3 protease having serine protease activity comprising an amino acid sequence numbered according to SEQ ID No.2 wherein the amino acid at position 156 is substituted with a non-alanine amino acid.

20. (New) The variant protease according to claim 1, wherein said amino acid at position 156 is selected from the group consisting of: glycine, threonine and valine.

21. (New) The variant protease according to claim 1, wherein said amino acid sequence comprises SEQ ID No.2, and further comprises at least one substitution selected from the

AMENDMENT
US APPLN. NO. 11/034,281

group consisting of: A156G; A156T; and A156V.

22. (New) The variant protease according to claim 1 or 2, further comprising a P89S substitution.

23. (New) A variant HCV NS3 protease which is at least 90% identical to amino acid sequence of SEQ ID No.2, comprising at least one substitution selected from the group consisting of: A156G; A156T; and A156V.

24. (New) The variant protease according to claim 5, further comprising a P89S substitution.